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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,651	09/15/2003	Bart De Strooper	2676-6086US	2464

24247 7590 02/07/2006

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EXAMINER	
EMCH, GREGORY S	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 02/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/662,651	STROOPER ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30,32-44,46 and 49-53* is/are pending in the application.

4a) Of the above claim(s) *1-30, 32-43 and 51-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44,46,49 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence alignments F-H*.

DETAILED ACTION

Formal Matters

Claims 30, 44 and 46 were amended, new claims 49-53 were added, and claims 31, 45, 47 and 48 were canceled in the communication dated 15 December 2005. Currently, claims 1-30, 32-44, 46 and 49-53 are pending. Claims 1-30, 32-43 and 51-53 are withdrawn from consideration as being directed to non-elected subject matter. Hence, claims 44, 46, 49 and 50 are under consideration.

Response to Amendment and Arguments

The objection to the specification is withdrawn in response to Applicant's amendment in the Response filed 15 December 2005.

The certified copy of application 01201015.3 filed in the European patent Office on March 16, 2001 has been received and entered in full.

The rejection of claims 31, 45, 47 and 48 under 35 U.S.C. 102(b) as being anticipated by Wadsworth et al. is rendered moot by cancellation of the claims and is thus withdrawn.

The rejection of claims 44 and 46 under 35 U.S.C. 102(b) as being anticipated by Wadsworth et al. is withdrawn in view of Applicant's amendments and arguments in the Response filed 15 December 2005.

At p.14 of the Response filed 15 December 2005, Applicant requests that claim 32 be rejoined and considered, since Applicant believes claim 44 is in condition for

allowance. Applicant's argument has been fully considered and is not found persuasive, since as set forth *infra*, claim 44 is not allowable.

New issues are set forth below.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections - 35 USC § 112, first paragraph

Claims 44 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of SEQ ID NOs: 7 or 12, does not reasonably provide enablement for compounds comprising SEQ ID NOs: 7 or 12.

The claims are drawn to a compound capable of modulating the interaction between a complex of a presenilin and a type I transmembrane protein, said compound comprising: a compound selected from the group consisting of SEQ ID NO: 7 and SEQ ID NO: 12 and a pharmaceutical compound comprising SEQ ID NOs: 7 or 12.

The claims are overly broad in the recitation of "comprising" since insufficient guidance is provided as to which of the myriad of molecular species encompassed by the claims will retain the characteristics of modulating the interaction between a complex of a presenilin and a type I transmembrane protein.

As an example of the unpredictable effects of mutations on protein function, Mickle et al. teaches that cystic fibrosis is an autosomal recessive disorder caused by

abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, de1ta-F508, a single phenylalanine is deleted at position 508, giving rise to the CF phenotype, thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

Additionally, Yan et al. teaches that in certain cases, a change of two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. *Science* 290: 523-527, 2000).

Furthermore, in the communication dated 15 December 2005, Applicant's states, "as is well known in the biological arts, the addition of more than 170% additional amino

acid sequence to a polypeptide can have drastic consequences in terms of overall function" (p.14). Accordingly, the claims as currently recited could have 170% additional amino acids, thus drastically affecting the function of the claimed compounds.

Since the claim encompasses polypeptides that comprise SEQ ID NOs: 7 or 12, and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Since the amino acid sequence of a polypeptide determines its structural and functional properties and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention. Given the large number of possible species encompassed by the claims, and the insufficient guidance provided in the specification, it would require undue experimentation of one of skill in the art to make and use the claimed invention.

Claims 44 and 49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Applicant is directed to

the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to a compound capable of modulating the interaction between a complex of a presenilin and a type I transmembrane protein, said compound comprising: a compound selected from the group consisting of SEQ ID NO: 7 and SEQ ID NO: 12 and a pharmaceutical compound comprising SEQ ID NOs: 7 or 12.

The claims set forth a multitude of potential molecules encompassed by the invention. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to how to make the claimed compounds. Structural features that could distinguish compounds in the genus from others in the molecular class are missing from the disclosure. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

The skilled artisan cannot envision all of the amino acid sequences that comprise SEQ ID NOs: 7 or 12 or all of the pharmaceutical compositions that comprise SEQ ID NOs: 7 or 12, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, any compound or composition comprising SEQ ID NOs: 7 or 12 is insufficient to describe the genus. Only

compounds or compositions consisting of SEQ ID NOs: 7 or 12, said compounds possessing the ability to modulate the interaction between a complex of a presenilin and a type I transmembrane protein meet the written description provision of 35 U.S.C. § 112, first paragraph. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

Claims 46 and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,187,153 to Cordell et al.

The claims are drawn to a compound capable of modulating the interaction between a complex of a presenilin and a type I membrane protein, said compound consisting essentially of: a compound selected from the group consisting of SEQ ID NO: 5, SEQ ID NO: 8, and SEQ ID NO: 13 and a pharmaceutical composition comprising said compound.

The '153 patent discloses a polypeptide with an amino acid sequence, which is 100% identical to Applicant's SEQ ID NOs: 5, 8 and 13 (see attached sequence alignments F-H). Although the polypeptides of the '153 patent are larger than Applicant's SEQ ID NOs: 5, 8 and 13, said patent discloses that the polypeptides of the invention include fragments of full-length β-amyloid proteins, β-amyloid related proteins, or muteins thereof (col. 6, lines 1-37). Also, the '153 patent discloses pharmaceutical compositions (col. 5, line 48 and col. 15 lines 60-66). Thus, since the patent discloses

all the elements of the claims, claims 46 and 50 are anticipated by U.S. Patent No. 5,187,153 to Cordell et al.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 8:30AM to 5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gregory S. Emch, Ph. D.
Patent Examiner
Art Unit 1649
February 2, 2006

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER

10/662,651
Sequence alignment F

SEQ ID NO: 5

RESULT 6
5187153-8
;Patent No. 5187153
; APPLICANT: CORDELL, BARBARA;SCHILLING, JAMES W.;KATUNUMA, NOBUHIKO
; TITLE OF INVENTION: METHODS OF TREATMENT USING ALZHEIMER'S
;AMYLOID POLYPEPTIDE DERIVATIVES
; NUMBER OF SEQUENCES: 33
; CURRENT APPLICATION DATA:
;   APPLICATION NUMBER: US/07/502,273
;   FILING DATE: 29-MAR-1990
; PRIOR APPLICATION DATA:
;   APPLICATION NUMBER: 361,912
;   FILING DATE: 06-JUN-1989
;   APPLICATION NUMBER: 359,911
;   FILING DATE: 12-MAY-1989
;   APPLICATION NUMBER: 87,002
;   FILING DATE: 18-AUG-1987
;   APPLICATION NUMBER: 8,810
;   FILING DATE: 30-JAN-1987
;   APPLICATION NUMBER: 948,376
;   FILING DATE: 31-DEC-1986
;   APPLICATION NUMBER: 932,193
;   FILING DATE: 17-NOV-1986
;SEQ ID NO:8:
;   LENGTH: 97
5187153-8

  Query Match   100.0%; Score 48; DB 6; Length 97;
  Best Local Similarity   100.0%; Pred. No. 0.1;
  Matches   11; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

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Qy          1 TVIVITLVMLK 11
              ||||||||||| 
Db         41 TVIVITLVMLK 51
```

10/662,651
Sequence alignment G

SEQ ID NO: 8

RESULT 2
5187153-8
;Patent No. 5187153
; APPLICANT: CORDELL, BARBARA;SCHILLING, JAMES W.;KATUNUMA, NOBUHIKO
; TITLE OF INVENTION: METHODS OF TREATMENT USING ALZHEIMER'S
;AMYLOID POLYPEPTIDE DERIVATIVES
; NUMBER OF SEQUENCES: 33
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/07/502,273
; FILING DATE: 29-MAR-1990
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 361,912
; FILING DATE: 06-JUN-1989
; APPLICATION NUMBER: 359,911
; FILING DATE: 12-MAY-1989
; APPLICATION NUMBER: 87,002
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; FILING DATE: 30-JAN-1987
; APPLICATION NUMBER: 948,376
; FILING DATE: 31-DEC-1986
; APPLICATION NUMBER: 932,193
; FILING DATE: 17-NOV-1986
;SEQ ID NO:8:
; LENGTH: 97
5187153-8

Query Match 100.0%; Score 79; DB 6; Length 97;
Best Local Similarity 100.0%; Pred. No. 3.7e-05;
Matches 18; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 VVIATVIVITLVMLKKKQ 18
              ||||||||||||||||||
Db         37 VVIATVIVITLVMLKKKQ 54
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10/662,651
Sequence alignment H

SEQ ID NO: 13

RESULT 2
5187153-8
;Patent No. 5187153
; APPLICANT: CORDELL, BARBARA;SCHILLING, JAMES W.;KATUNUMA, NOBUHIKO
; TITLE OF INVENTION: METHODS OF TREATMENT USING ALZHEIMER'S
;AMYLOID POLYPEPTIDE DERIVATIVES
; NUMBER OF SEQUENCES: 33
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: US/07/502,273
; FILING DATE: 29-MAR-1990
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: 361,912
; FILING DATE: 06-JUN-1989
; APPLICATION NUMBER: 359,911
; FILING DATE: 12-MAY-1989
; APPLICATION NUMBER: 87,002
; FILING DATE: 18-AUG-1987
; APPLICATION NUMBER: 8,810
; FILING DATE: 30-JAN-1987
; APPLICATION NUMBER: 948,376
; FILING DATE: 31-DEC-1986
; APPLICATION NUMBER: 932,193
; FILING DATE: 17-NOV-1986
;SEQ ID NO:8:
; LENGTH: 97
5187153-8

Query Match 100.0%; Score 67; DB 6; Length 97;
Best Local Similarity 100.0%; Pred. No. 0.00026;
Matches 15; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy          1 ATVIVITLVMLKKKQ 15
              |||||||||||||||
Db         40 ATVIVITLVMLKKKQ 54
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